We claim:

1. A multiple inducible gene modulation system comprising a plurality of individually operable gene modulation systems wherein:

a) each individually operable gene modulation system comprises:

i) one or more polynucleotides encoding a receptor complex comprising:

A) a DNA binding domain;

B) a ligand binding domain; and

C) a transactivation domain;

ii) a ligand;

iii) a polynucleotide comprising:

A) an exogenous or endogenous polynucleotide; and

B) a response element;

wherein:

A) the exogenous or endogenous polynucleotide is operatively linked to the response element; and

B) binding of the DNA binding domain to the response element in the presence or absence of the ligand results in activation or suppression of the exogenous or endogenous polynucleotide; and

b) each individually operable gene modulation system is orthogonal to the other individually operable gene modulation system present in the multiple inducible gene modulation system.

2. The multiple inducible gene expression system of claim 1, wherein each operable gene expression modulation system comprises

a) i) a first gene expression cassette comprising a polynucleotide that encodes a polypeptide comprising a transactivation domain, a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and a nuclear receptor ligand binding domain,

ii) a ligand, and

iii) a second gene expression cassette comprising: A) a response element recognized by the DNA-binding domain of the encoded polypeptide of the first gene expression cassette; B) a promoter that is activated by the transactivation domain of the encoded polypeptide of the first gene expression cassette; and C) a gene whose expression is to be modulated;

b) i) a first gene expression cassette comprising a polynucleotide that encodes a polypeptide comprising a transactivation domain, a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and a nuclear receptor ligand binding domain,

ii) a second nuclear receptor ligand binding domain selected from the group consisting of a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, an ultraspiracle protein ligand binding domain, and a chimeric ligand binding domain comprising two polypeptide fragments, wherein the first polypeptide fragment is from a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, or an ultraspiracle protein ligand binding domain, and the second polypeptide fragment is from a different vertebrate retinoid X receptor ligand binding domain, invertebrate retinoid X receptor ligand binding domain, or ultraspiracle protein ligand binding domain,

iii) a ligand, and

iv) a second gene expression cassette comprising: A) a response element recognized by the DNA-binding domain of the encoded polypeptide of the first gene expression cassette; B) a promoter that is activated by the transactivation domain of the encoded polypeptide of the first gene expression cassette; and C) a gene whose expression is to be modulated; or

c) i) a first gene expression cassette comprising a polynucleotide that encodes a first polypeptide comprising a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated and a nuclear receptor ligand binding domain,

ii) a second gene expression cassette comprising a polynucleotide that encodes a second polypeptide comprising a transactivation domain and a nuclear receptor ligand binding domain,

iii) a ligand, and

iv) a third gene expression cassette comprising: A) a response element recognized by the DNA-binding domain of the first polypeptide of the first gene expression cassette; B) a promoter that is activated by the transactivation domain of the second polypeptide of the second gene expression cassette; and C) a gene whose expression is to be modulated,

wherein one of the nuclear receptor ligand binding domains of c)i) or c)ii) is a Group

H nuclear receptor ligand binding domain.

3. A virus comprising the multiple gene regulation system of claim 1.

4. A cell comprising the multiple gene regulation system of claim 1.

5. A transgenic organism comprising one or more cells of claim 4.

6. The multiple inducible gene regulation system of claim 1, wherein one or more of the polynucleotides encoding a receptor complex encodes a nuclear receptor complex.

7. The multiple inducible gene regulation system of claim 1, wherein one or more of the polynucleotides encoding a receptor complex encodes a non-mammalian receptor complex.

8. The multiple inducible gene regulation system of claim 6, wherein the receptor complex is an ecdysone receptor complex.

9. A multiple inducible gene regulation system which comprises a plurality of individually operable gene regulation systems wherein:

a) each individually operable gene regulation system comprises:

i) one or more receptor complexes, each comprising:

A) a DNA binding domain;

B) a ligand binding domain; and

C) a transactivation domain;

ii) a ligand;

iii) a polynucleotide comprising:

A) an exogenous or endogenous gene; and

B) a response element;

wherein:

A) the exogenous or endogenous gene is under the control of the response element; and

B) binding of the DNA binding domain to the response element in the presence or the absence of the ligand results in activation or suppression of the gene; and

b) each individually operable gene regulation system is orthogonal to the other individually operable gene regulation systems present in the multiple inducible gene regulation system.

10. The multiple inducible gene expression system of claim 9, wherein each operable gene expression modulation system comprises

a) i) a polypeptide comprising a transactivation domain, a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and a nuclear receptor ligand binding domain,

ii) a ligand, and

iii) a gene expression cassette comprising: A) a response element recognized by the DNA-binding domain of the polypeptide of a)i); B) a promoter that is activated by the transactivation domain of the polypeptide of a)i); and C) a gene whose expression is to be modulated;

b) i) a polypeptide comprising a transactivation domain, a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and a nuclear receptor ligand binding domain,

ii) a second nuclear receptor ligand binding domain selected from the group consisting of a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, an ultraspiracle protein ligand binding domain, and a chimeric ligand binding domain comprising two polypeptide fragments, wherein the first polypeptide fragment is from a vertebrate retinoid X receptor ligand binding domain, an invertebrate retinoid X receptor ligand binding domain, or an ultraspiracle protein ligand binding domain, and the second polypeptide fragment is from a different vertebrate retinoid X receptor ligand binding domain, invertebrate retinoid X receptor ligand binding domain, or ultraspiracle protein ligand binding domain,

iii) a ligand, and

iv) a gene expression cassette comprising: A) a response element recognized by the DNA-binding domain of the polypeptide of b)i); B) a promoter that is activated by the transactivation domain of the polypeptide of b)i); and C) a gene whose expression is to be modulated; or

c) i) a first polypeptide comprising a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated and a nuclear receptor ligand binding domain,

ii) a second polypeptide comprising a transactivation domain and a nuclear receptor ligand binding domain,

iii) a ligand, and

iv) a gene expression cassette comprising: A) a response element recognized by the DNA-binding domain of the first polypeptide of c)i); B) a promoter that is activated by the transactivation domain of the second polypeptide of c)ii); and C) a gene whose expression is to be modulated,

wherein one of the nuclear receptor ligand binding domains of c)i) or c)ii) is a Group H nuclear receptor ligand binding domain.

11. A virus comprising the multiple gene regulation system of claim 9.

12. A cell comprising the multiple gene regulation system of claim 9.

13. A transgenic organism comprising one or more cells of claim 12.

14. The multiple inducible gene regulation system of claim 9, wherein one or more of the receptor complexes is a Group H receptor complex.

15. The multiple inducible gene regulation system of claim 14, wherein the Group H receptor complex is an ecdysone receptor complex.

16. A method to develop a multiple gene regulation system comprising the steps of:

a) defining a set of diversely-modified ligands based on incremental pharmacophore element changes;

b) preparing a first set of receptor polypeptides, wherein each receptor polypeptide comprises a ligand binding domain that is:

i) naturally occurring;

ii) modified by deletion, insertion, or mutation;

iii) chimeric;

iv) synthetic; or

v) a combination thereof;

c) optionally, introducing the receptor polypeptides into a cell;

d) querying the receptor polypeptides either in the cell of c) or *in vitro*, with the set of diversely-modified ligands for gene modulation, or ligand binding domain binding, or both;

e) determining the orthogonality of the receptor polypeptide/ligand combinations to define a subset of ligands with diverse gene modulation properties;

f) optionally repeating steps a)-e) using a modified set of ligands and a modified set of receptor polypeptides;

g) preparing a second set of receptor polypeptides, wherein each receptor polypeptide comprises a DNA binding domain that is:

i) naturally occurring;

ii) modified by deletion, insertion, or mutation;

iii) chimeric;

iv) synthetic; or

v) a combination thereof;

h) preparing a set of DNA constructs comprising an exogenous or endogenous gene and response elements which are:

i) naturally occurring;

ii) modified by deletion, insertion, or mutation;

iii) chimeric;

iv) synthetic; or

v) a combination thereof;

i) cloning the first set of receptor polypeptides and the second set of receptor polypeptides and the DNA constructs and then introducing the clones into a cell;

j) assaying the cell for coreactivity to the ligands identified in step e);

k) selecting an orthogonal set of ligands, ligand binding domains, DNA binding domains, and response elements based upon the results of steps e) and j) to comprise the multiple inducible gene regulation system.

17. The method of claim 16, wherein one or more of the receptor polypeptides is a nuclear receptor polypeptide.

18. The method of claim 17, wherein one or more of the receptor polypeptides is a non-mammalian receptor polypeptide.

19. The method of claim 17, wherein one or more of the nuclear receptor polypeptides is a group H nuclear receptor polypeptides.

20. The method of claim 17, wherein one or more of the nuclear receptor polypeptides is an ecdysone receptor polypeptides.